LITESPARK 033
ONCOLOGY CLINICAL TRIALS

Learn about a clinical trial for renal cell carcinoma (RCC)

In this brochure, you will learn about **renal cell carcinoma (RCC)** and a clinical trial for this disease. In this trial, researchers are trying to find out if the investigational combination of study drugs are safe and may help slow down or stop your RCC from spreading to other areas of the body.

You can also use this brochure to talk with your doctor about this trial.

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What is renal cell carcinoma (RCC)?

Renal cell carcinoma (RCC) is the most common type of kidney cancer, which is a cancer that starts in the kidney. It is also called renal cell cancer or renal cell adenocarcinoma. RCC usually grows as a single tumor in 1 kidney, but sometimes as 2 or more tumors in 1 kidney, or tumors in both kidneys at the same time.

What are my treatment options?

If you have RCC your care team will talk about your treatment options with you and those close to you. Your options will depend on a few things:

- Your overall health
- The stage of your cancer, which tells you if the cancer has spread and how far
- Chance of the cancer coming back
- Side effects you might have from the treatment
- What chance the treatment has of slowing down or stopping the cancer
- How long the treatment might help extend your life
- How much the treatment might help improve your symptoms
- Features of your cancer cells (called biomarkers) that may help guide your treatment

Your care team may offer you 1 or more of these treatments:

- **Local therapies** – treatment directed at the site of the cancer to destroy it

- **Targeted therapy** – treatment that works on specific cells to stop them from growing
- **Immunotherapy** – medicines that help your immune system fight the cancer
- **Chemotherapy** – medicine to kill cancer cells or stop them from growing
- **Radiation therapy** – treatment that uses beams of intense energy (like X-rays) to shrink or get rid of tumors. This would only be used to treat symptoms related to tumor growth.
- **Palliative care** – also called comfort care. This is special care to help ease pain and symptoms with a focus on the person's quality of life. This does not directly treat RCC, but it helps keep you as comfortable as possible.
- **Surgery** – treatment to remove all or part of the cancer
- **Watchful waiting** – your care team might wait and watch the cancer before they use any treatment (also called active surveillance)
- **Clinical trials**, such as this one

Talk to your doctor to find out which treatment is right for you.

What is a clinical trial?

Clinical trials are research studies that help doctors find out if study drugs (alone or with other treatments) are safe and if they can help prevent, find, or treat diseases or conditions. Clinical trials are carefully controlled research studies that are done to get a closer look at investigational treatments and procedures.

All about this clinical trial

What is the goal of this clinical trial?

The goal of this trial is to learn if the investigational combination of the study drugs, belzutifan and zanzalintinib, are safe to use and may help slow down or stop the growth of RCC.

Researchers will compare the investigational combination of belzutifan and zanzalintinib to a standard treatment for RCC, called cabozantinib. Researchers don't know if the investigational combination of belzutifan and zanzalintinib may help treat RCC.

What treatment is being studied?

The investigational study drug is belzutifan (also called MK-6482). Researchers will test it together with another investigational study drug, zanzalintinib.

Belzutifan is an experimental drug. It has been approved by some health authorities for treating some types of cancer, including RCC in adults with a rare disease called von Hippel-Lindau (VHL). It may not be approved in your country for your type of cancer.

Zanzalintinib is an experimental drug and has not been approved, either alone or in combination with belzutifan for the treatment of advanced RCC.

About Belzutifan:

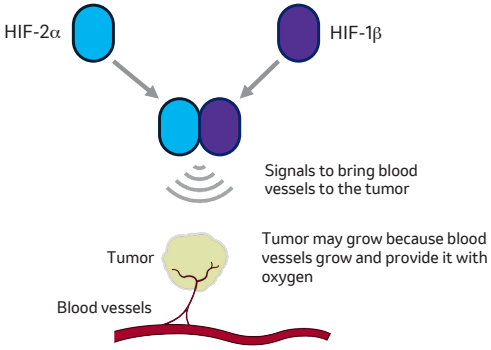
Belzutifan (also known as MK-6482) is an investigational study drug that may help stack cancer cells. Belzutifan is approved in some countries to treat some types of RCC.

1. The hypoxia-inducible factor, HIF-2*α*, is believed to play a critical role in tumor creations and tumor progression in cancers such as pheochromocytomas and paragangliomas (PPGL)and renal cell carcinoma.
2. When the body experiences hypoxia (low oxygen), HIF-2*α* and HIF-1β can bind together and cause the increased creation of red blood cells and blood vessels that go to the tumor and help it grow. This also may prevent the cell from naturally dying on its own.
3. The study drug Belzutifan comes in and stops HIF-2*α* and HIF-1β from binding to each other.
4. This study is evaluating whether blocking the binding of HIF-2*α* and HIF-1β will allow the cell to naturally go through its lifecycle, die off and cause the tumor cells to stop growing.

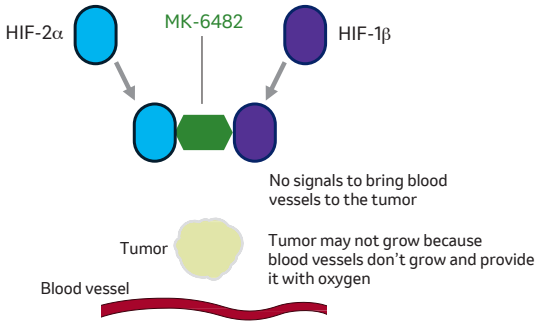


Deciding to join a clinical trial is something only you, those close to you, and your care team can decide together. If there is anything you do not understand, ask the trial doctor.

Another way to think about Belzutifan



When HIF-2αand HIF-1β bind together, it brings oxygen and blood to tumor cells. This helps cancer cells grow and survive.



This clinical trial looks at whether Belzutifan can block HIF-2*α* and HIF-1β from binding, so that the cancer cells don't get oxygen and blood.

Who can join this trial?

There are eligibility criteria that will determine if you will quality for participation. For example, you must:

- Be at least 18 years old
- Have RCC that has come back and spread to other parts of the body within 2 years of receiving initial treatment for RCC

Your trial staff will do tests to see if you are able to join this trial.

You and your trial doctor will discuss:

- All the requirements to join this trial
- Possible benefits, risks, and side effects of being in this trial

If I join, how long will I be in the trial?

How long you will be in the trial depends on:

- Your health
- How well you tolerate the study treatments

What will happen during trial visits?

You will visit the trial site on a regular schedule so that the trial doctors can see how the study drugs are working for you. During your trial visits, you may get:

- Your assigned study drug
- Blood and urine tests
- Physical exams
- Survey questions about how you are feeling
- ECG (electrocardiogram), ECHO (echocardiogram), and MUGA (multigated acquisition) scan (tests to see how well your heart is working)
- Imaging scans such as CT scans or MRIs (scans that help the doctor see the cancer inside your body)

You can ask your trial doctor any questions you have about what happens during trial visits and how often they will happen.

If you are able to join the trial, your trial doctor will need to stay in contact with you even after your trial visits are over. This is very important because this clinical trial is studying how well the study treatment works over time.

What treatments will I get?

The study drug you get will depend on which group you are randomly placed in. This trial has two groups:

- **Group 1** will get the investigational combination of belzutifan and zanzalitinib
- **Group 2** will get cabozantinib

A computer will decide which group you are put in. You have an equal chance of getting put in each group.

What is a tissue sample and why is it part of this trial?

If you are eligible and join the trial, the study doctor will ask you for tissue samples. Tissue, such as skin, hair, nails, blood, urine or tumors, are found in your body and are collected as they may help researchers understand diseases and find ways to help prevent and treat them in people.

For this study, your study doctor will collect tumor and blood tissue samples. These may be new tissue samples, or they may ask to use tissue that was collected before. Tissue you provide for the study will be stored for research only and will continue to be tracked according to your study code number.

If a new tissue sample is collected for this study, the study doctor will explain how it will be collected and any risks. Some risks include:

- Low blood pressure
- Pain
- Bruising
- Redness
- Swelling
- Scarring
- Infection
- Slight bleeding at biopsy site

There are also risks related to data privacy (please see frequently asked questions below) and the release of personal information from your health records.

Frequently asked questions about tissue collection

Will I find out the results of the research using my tissue?

This will depend on the reason for the tissue sample. You may see the results of your biomarker test (such as a biopsy or blood test) if it is required for you to join or impacts your current participation in the clinical trial. Results of tests performed only for research purposes will generally not be provided.

How is my privacy protected?

To protect your privacy, we take steps to limit the risk of anyone identifying you:

- We label your tissue with a number instead of your name
- We remove your name, address, phone number, social security number, date of birth and anything else that could directly identify you before researchers get access to your records or tissue sample.

If I agree to take part in the study, can I change my mind later?

Yes. You can change your mind about taking part in the trial at any time. Here's how:

1. Contact your study doctor and tell them you do not want to be in the study anymore.
2. The study doctor will contact the study Sponsor.

Tissue samples obtained up until the point of you withdrawing from the trial will continue to be retained to support the trial research.

Thank you for learning about RCC and this clinical trial

You can use this brochure to talk with your doctor about this trial.

To learn more

To learn more about this trial, you can

- Talk to your doctor
- Visit **www.merckoncologyclinicaltrials.com**
- Scan this QR code:

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MK-6482-033_PB_NA_English_V00.1_05Jun2025
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